INTRODUCTION TO DRUG UTILISATION RESEARCH

Methodological Framework and Skills Needs in Drug Utilization Research

DR LISA PONT

UNIVERSITY OF SYDNEY

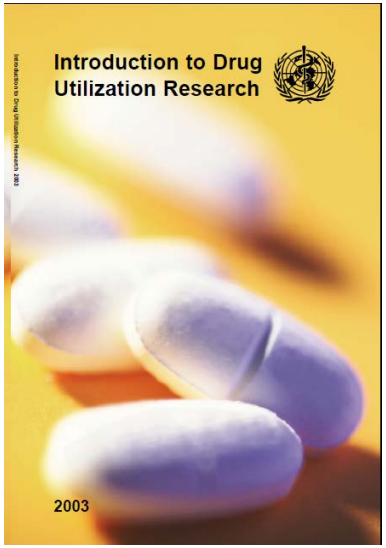
CHAIR MEDICINES USE RESEARCH AUSTRALIA (MURA)

CHAIR DRUG UTILISATION/ HEALTH SERVICES RESEARCH SIG

THE UNIVERSITY OF SYDNEY

Drug Utilization - traditional definition

The marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences (WHO 1977)



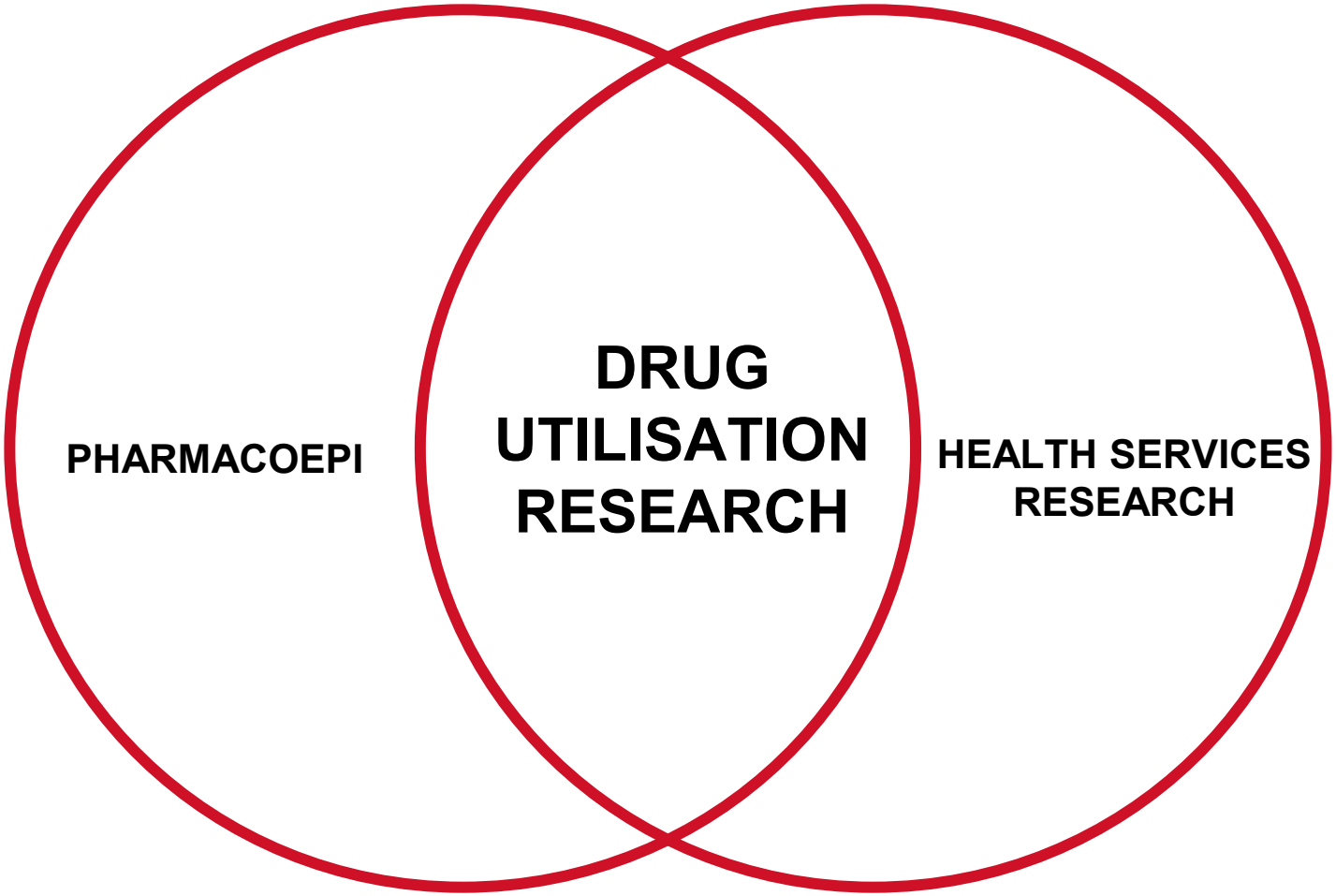
"An eclectic collection of descriptive and analytical methods for the quantification, the understanding and the evaluation of the processes of prescribing, dispensing and consumption of medicines, and for the testing of interventions to enhance the quality of these processes."

Wettermark et al. In Pharmcoepidemiology and Risk Management, Hartzema (ed) 2008

Related disciplines

Pharmacoepidemiology is the study of the use and effects of drugs in large numbers of people (Strom)

Health services research is a multidisciplinary field of inquiry, both basic and applied, that examines the use, costs, quality, accessibility, delivery, organization, financing, and outcomes of health care services to increase knowledge and understanding of the structure, processes, and effects of health services for individuals and populations (IOM, 1995)


PHARMACOEPI
DRUG UTILISATION RESEARCH
HEALTH SERVICES RESEARCH

Methodological framework for drug utilization research

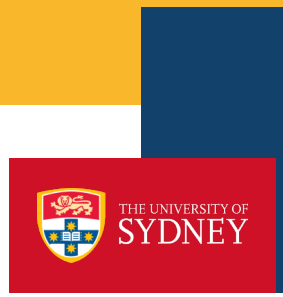
The micro level

Understanding prescribing behaviour and patient drug taking behaviour

The macro level

Comparisons of drug utilization

DUR: *Conceptual framework*



Conceptual framework for drug utilization research

	Quantify	Understand	Evaluate	Quality improvement
Prescribing				
Dispensing				
Consumption				

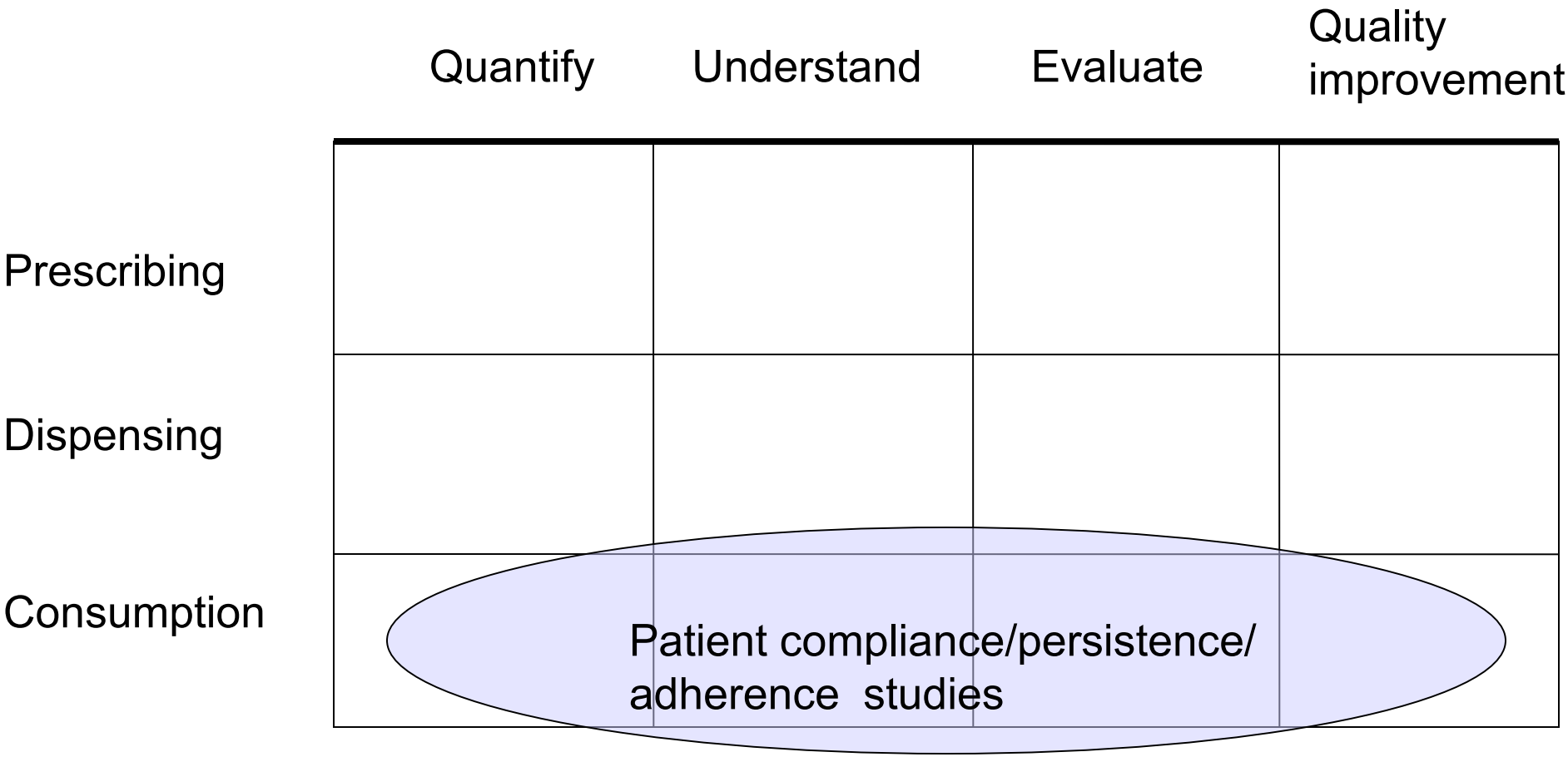
Conceptual framework for drug utilization research

	Quantify	Understand	Evaluate	Quality improvement
Prescribing				
Dispensing				
Consumption	Health surveys			

Conceptual framework for drug utilization research

	Quantify	Understand	Evaluate	Quality improvement
Prescribing		Drug choice and decision making		
Dispensing				
Consumption				

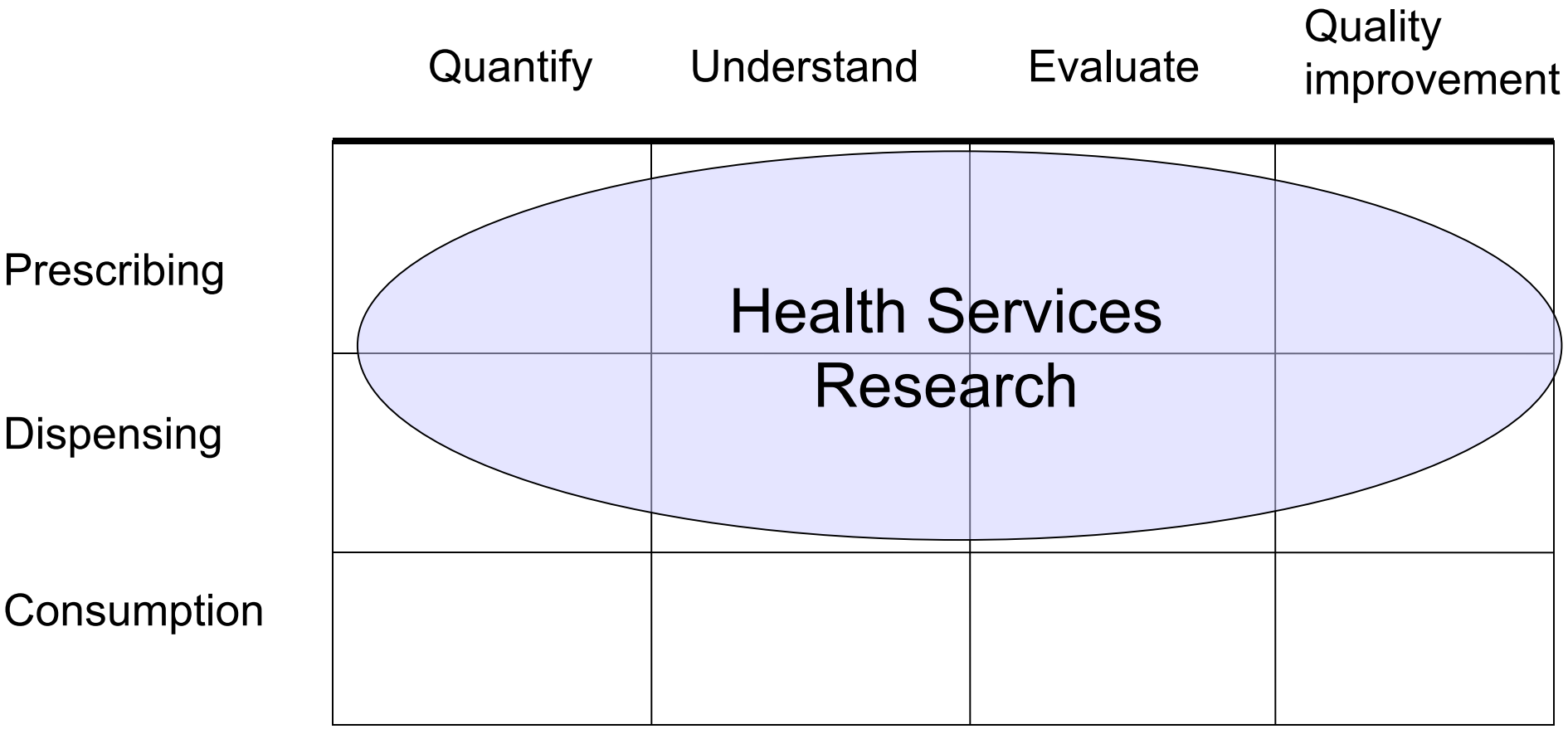
Conceptual framework for drug utilization research



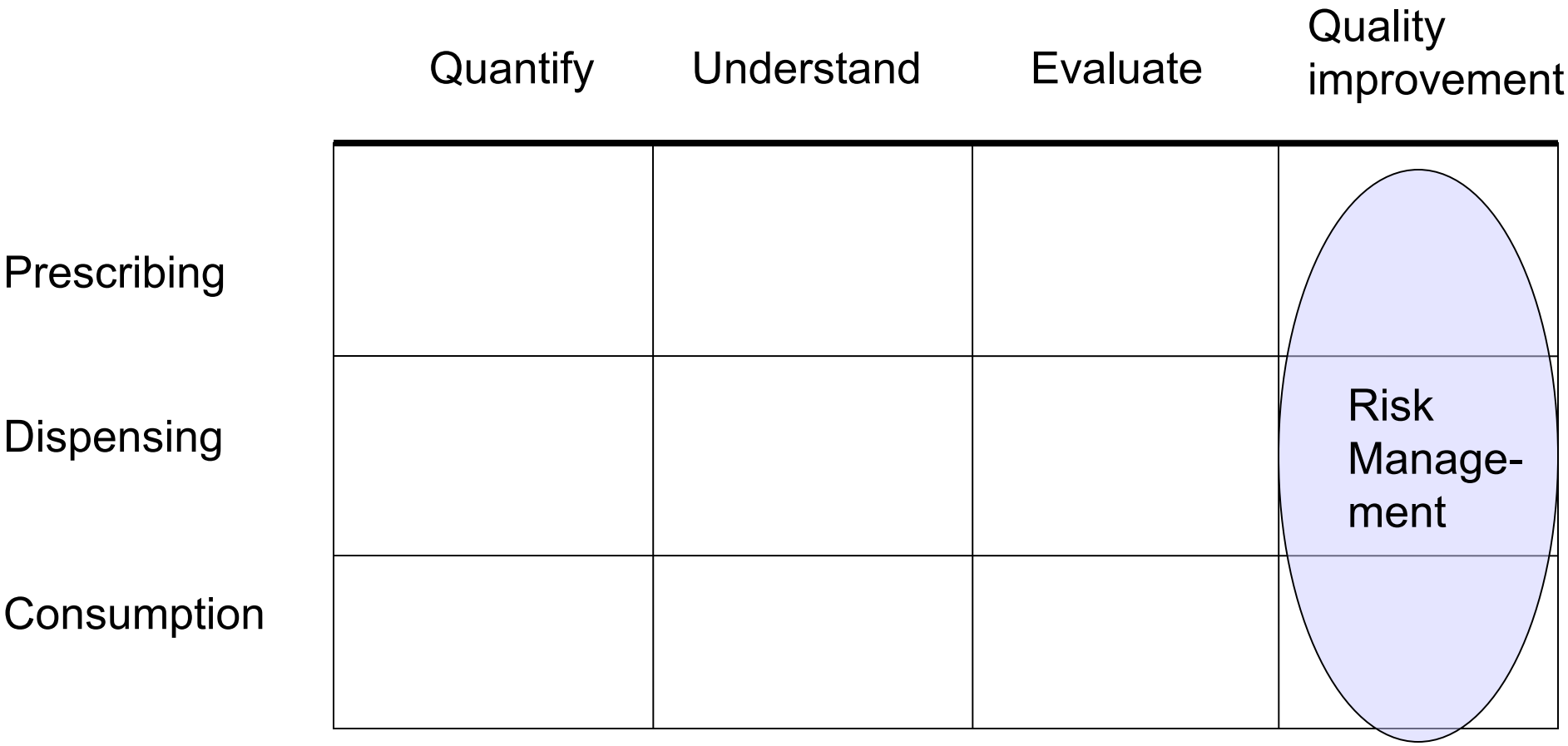
	Quantify	Understand	Evaluate	Quality improvement
Prescribing			Prescribing quality indicators	
Dispensing				
Consumption				

	Quantify	Understand	Evaluate	Quality improvement
Prescribing				Individual prescription feedback
Dispensing				
Consumption				

Conceptual framework for drug utilization research



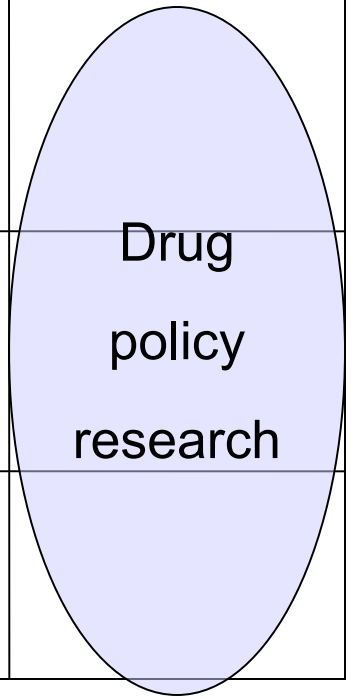
Conceptual framework for drug utilization research

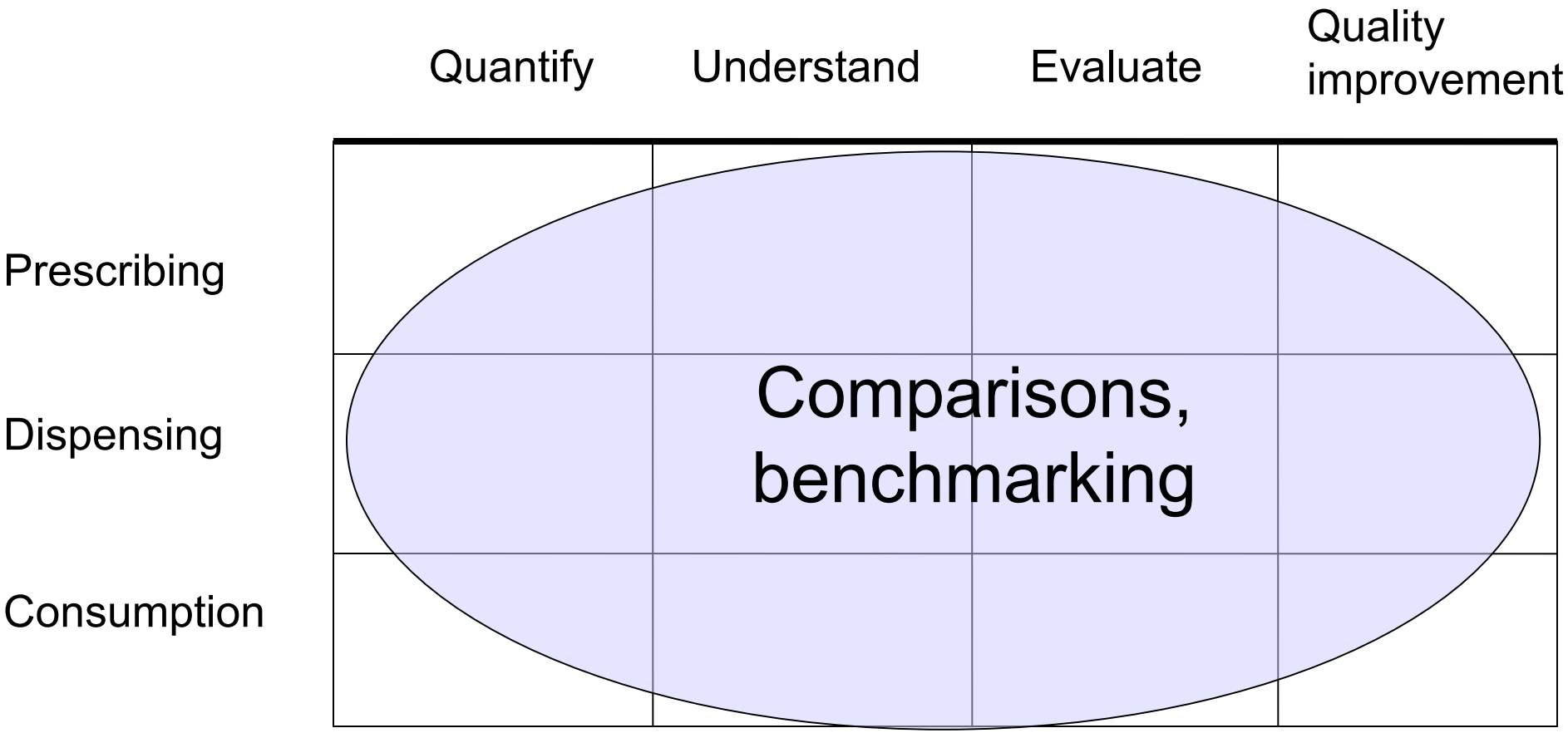


Conceptual framework for drug utilization research

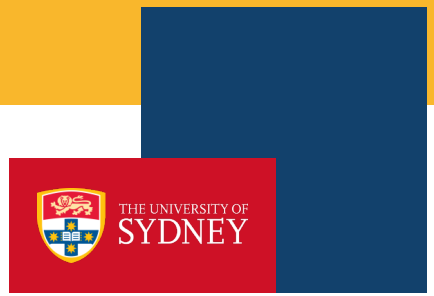
	Quantify	Understand	Evaluate	Quality improvement
Prescribing				
Dispensing				
Consumption				Patient education

	Quantify	Understand	Evaluate	Quality improvement
Prescribing				
Dispensing				
Consumption				




Quantify
Understand
Evaluate
Quality improvement
Prescribing
Dispensing
Consumption
Comparisons, benchmarking

Drug utilization research: Skills needed



Quantifying drug utilization

> *"An eclectic collection of descriptive and analytical methods for the **quantification**, the understanding and the evaluation of the **processes of prescribing, dispensing and consumption of medicines**, and for the testing of interventions to enhance the quality of these processes."*

- Understanding different data sources
  - Administrative datasets
    - Contents, validity
  - Individual data collection
    - Patient/prescriber
      - questionnaires, interviews, electronic monitoring devices…
- Prescribing & reimbursement regulations
- Principles of clinical pharmacology
  - Quality Use of Medicines, guidelines, critical drug evaluation

Potential datasources

Wholesaler

Industry

Claims and reimbursement databases

Individual data collection

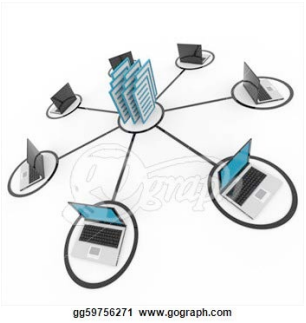
(prescribers/patients)

Medical records

Pharmacy databases

Hospital/ administration records

Disease based registers



Taxonomy and terminology

- Classification systems
  - ATC, IDIS, SNOWMED
- Measurement units
  - DDD, patients, expenditure, prescriptions
- Individual usage patterns
  - persistence, switching, commencement, cessation
- Epidemiological study designs
  - ecological studies, cohort studies, case-control studies, case crossover studies
- Epidemiological terminology
  - prevalence, incidence, exposure, outcome, relative risk, odds ratio, bias, confounding
- Biostatistical methods
  - descriptive statistics, sampling, significance, correlation, regression analyses

Understanding drug utilization

"An eclectic collection of descriptive and analytical ***methods for*** *the quantification,* ***the understanding*** *and the evaluation of the processes of prescribing, dispensing and consumption of medicines, and for the testing of interventions to enhance the quality of these processes."*

- Qualitative methods
  - in depth interviews, focus group discussions, observations
  - phenomenology, grounded theory, qualitative content analysis, narrative analysis
- Quantitative methods
  - Purposive sampling
  - Data triangulation
  - Consensus methods
    - Delphi, RAND, nominal group techniques, consensus development

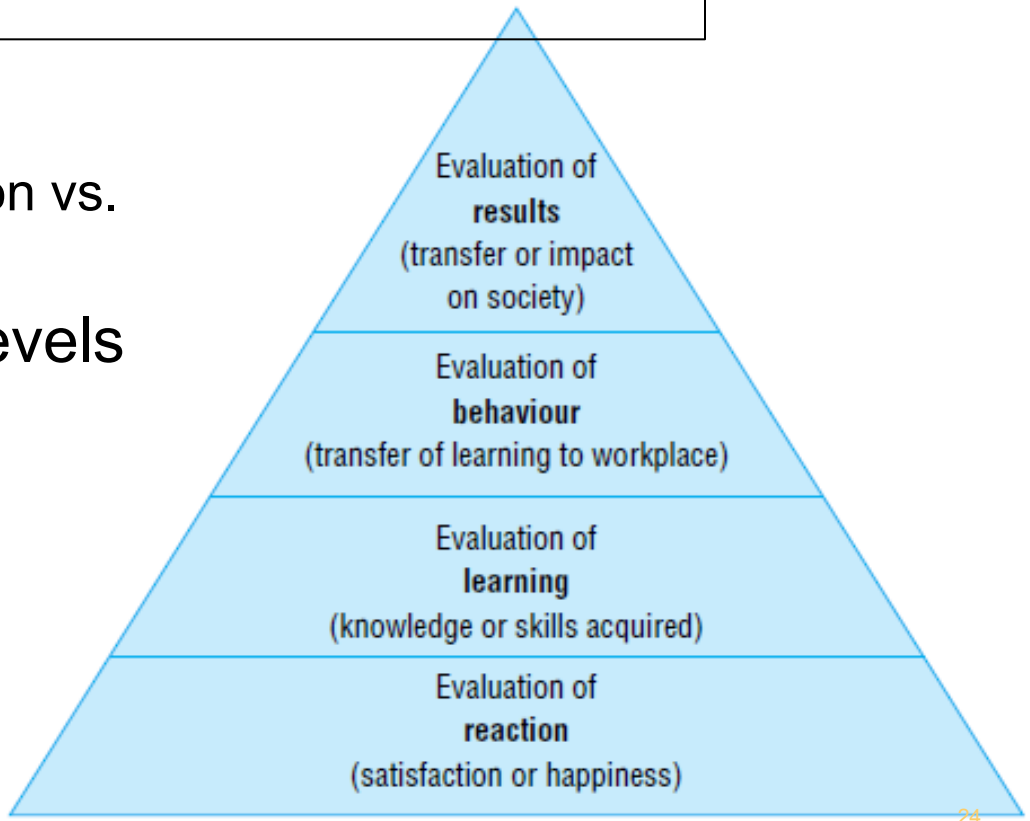
Evaluating drug utilization

*"An eclectic collection of descriptive and analytical **methods for** the quantification, the understanding and **the evaluation** of the processes of prescribing, dispensing and consumption of medicines, and for the testing of interventions to enhance the quality of these processes."*

› Evaluation techniques

- Single user-focused evaluation vs. scientific research evaluation

› Kirkpatrick´s hierarchial levels of evaluation



Interventions to change drug utilization

*"An eclectic collection of descriptive and analytical methods for the quantification, the understanding and the evaluation of the processes of prescribing, dispensing and consumption of medicines, and for the **testing of interventions** to enhance the quality of these processes."*

- Implementation research
  - Study design
  - testing of interventions
    - CBA, RCT
- Implementation of strategies in practice
  - Quasi experimental study designs
    - CBA, time series analyses
- Cluster randomized trials

Quantifying and improving quality

"An eclectic collection of descriptive and analytical methods for the quantification, the understanding and the evaluation of the processes of prescribing, dispensing and consumption of medicines, and for the testing of interventions to ***enhance the quality*** *of these processes."*

- Understanding and defining quality
  - prescribing, dispensing and consumption of medicines?
- Quality assessment tools
  - Quality indicators
    - terminology, context, validation, use

STUDY DESIGNS IN DRUG UTILISATION

Quantitative designs

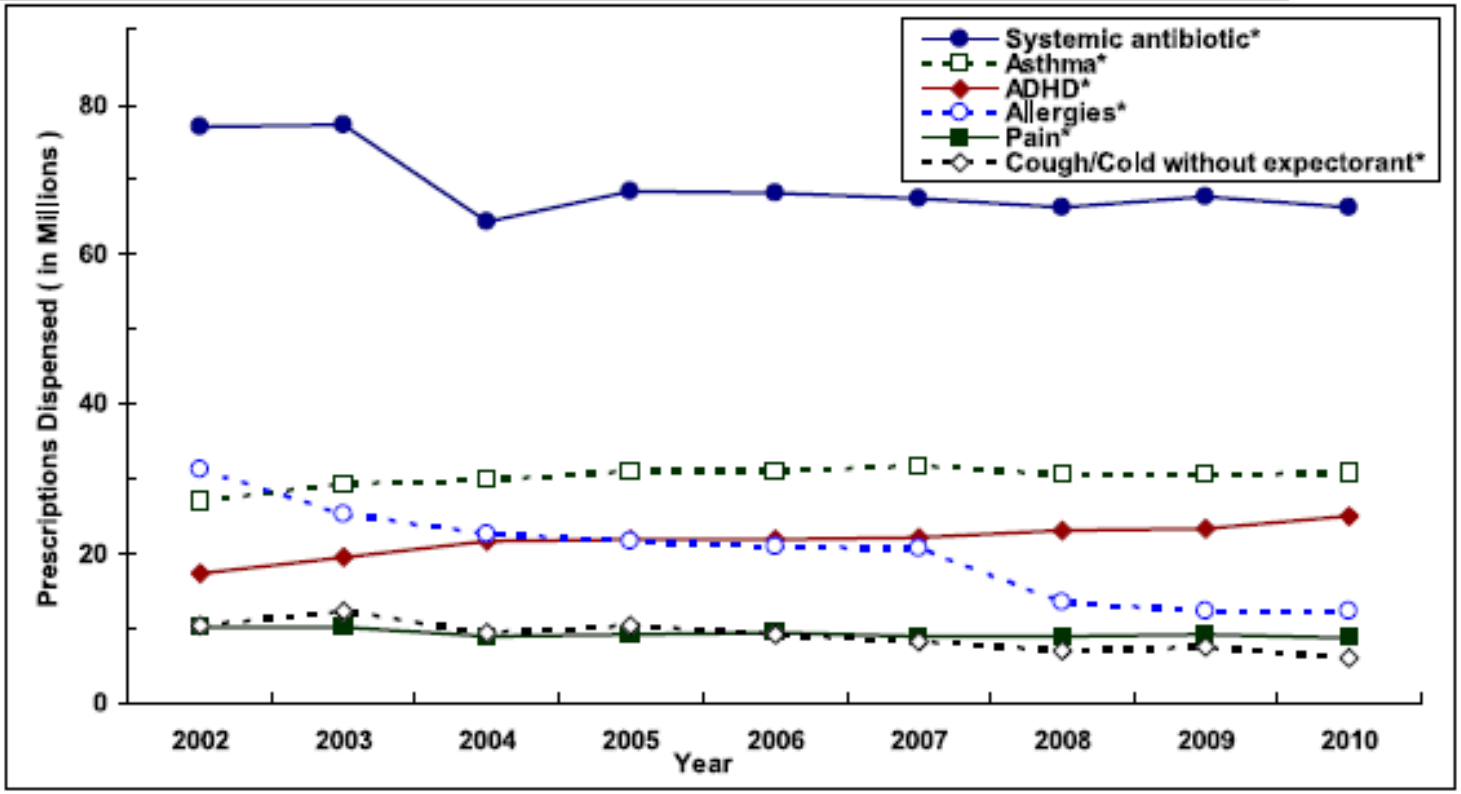
Descriptive

Analytical

Interventional

ARTICLE

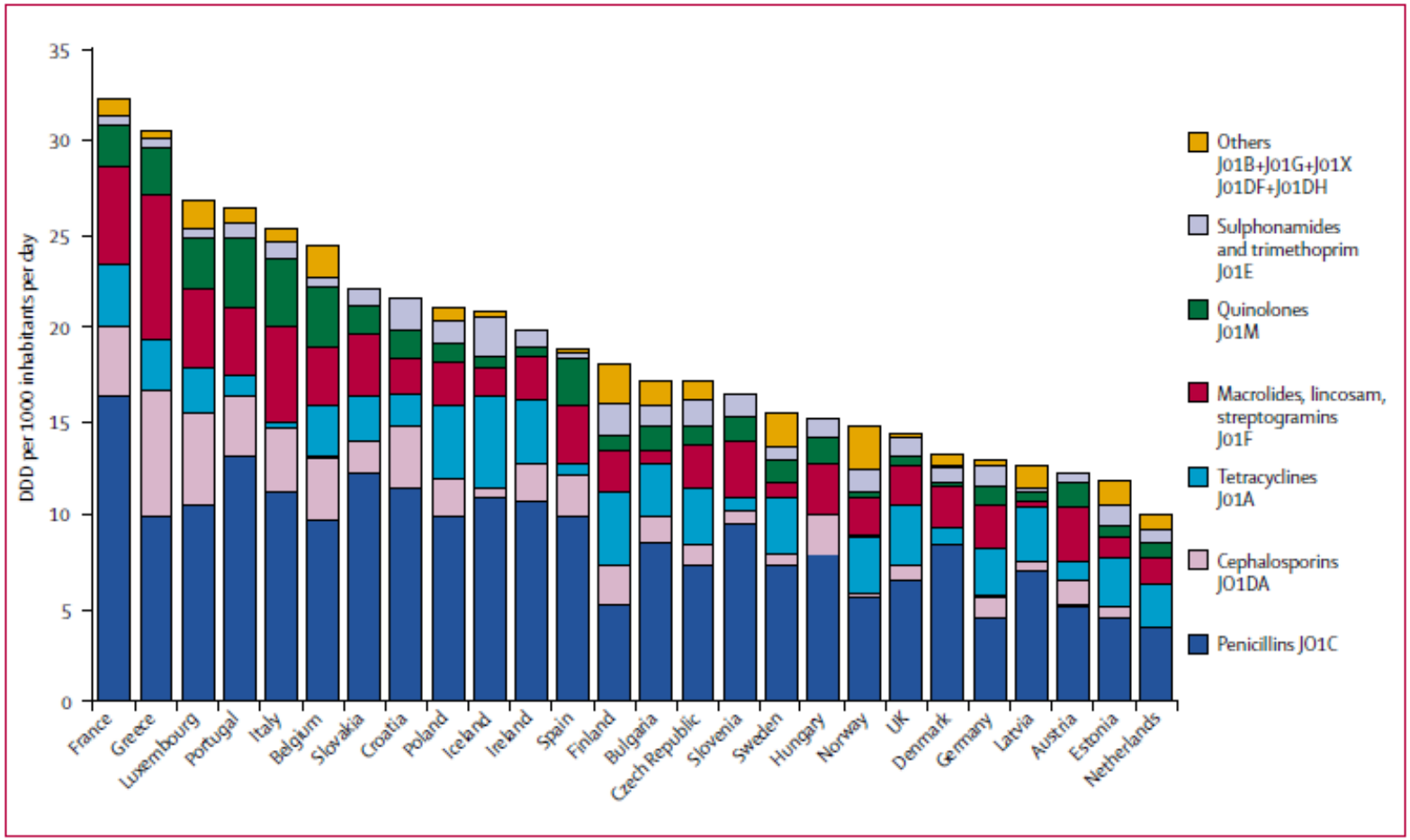
Trends of Outpatient Prescription Drug Utilization in US Children, 2002–2010



Chai et al. Pediatrics 2012

Outpatient antibiotic use in Europe and association with resistance: a cross-national database study

*Herman Goossens, Matus Ferech, Robert Vander Stichele, Monique Elseviers, for the ESAC Project Group**



Goosens et al. Lancet 2005

Sex Differences in Inappropriate Drug Use: a Register-Based Study of Over 600,000 Older People

Parameter	Women, n (%)	Men, n (%)
≥1 Indications of inappropriate drug use	95,613 (24.6)	49,787 (19.3)
Types of inappropriate drug use		
Anticholinergic drugs	33,658 (8.7)	16,397 (6.4)
urinary antispasmodics	11,350 (2.9)	6,356 (2.5)
nonselective monoamine reuptake inhibitors	8,775 (2.3)	2,646 (1.0)
hydroxyzine	7,225 (1.9)	3,790 (1.5)
Long-acting benzodiazepines	25,859 (6.7)	11,080 (4.3)
diazepam	10,431 (2.7)	4,886 (1.9)
flunitrazepam	10,084 (2.6)	4,257 (1.7)
nitrazepam	6,159 (1.6)	2,289 (0.9)
≥3 Psychotropic drugs	35,882 (9.2)	14,523 (5.6)
Potentially serious drug–drug interactions	26,000 (6.7)	18,486 (7.2)
Aspirin plus NSAIDs	16,140 (4.2)	11,059 (4.3)
Aspirin plus warfarin	1,303 (0.3)	1,850 (0.7)
Warfarin plus NSAIDs	1,349 (0.3)	1,397 (0.5)

NSAIDs = nonsteroidal antiinflammatory drugs.
[a]N = 387,951 women and 257,478 men.

nappropriate Drug Use in Women Compared with Men in Study Population[a]

Parameter	Odds Ratio (95% CI) Unadjusted	Adjusted[b]
≥1 Indications of inappropriate drug use	1.36 (1.35 to 1.38)	1.24 (1.23 to 1.26)
Anticholinergic drugs	1.40 (1.37 to 1.42)	1.29 (1.27 to 1.32)
urinary antispasmodics	1.19 (1.15 to 1.23)	1.13 (1.09 to 1.17)
nonselective monoamine reuptake inhibitors	2.23 (2.13 to 2.33)	2.06 (1.97 to 2.15)
hydroxyzine	1.27 (1.22 to 1.32)	1.11 (1.07 to 1.16)
Long-acting benzodiazepines	1.59 (1.55 to 1.62)	1.45 (1.42 to 1.49)
diazepam	1.43 (1.38 to 1.48)	1.30 (1.26 to 1.35)
flunitrazepam	1.59 (1.53 to 1.65)	1.45 (1.39 to 1.50)
nitrazepam	1.80 (1.71 to 1.89)	1.63 (1.55 to 1.71)
≥3 Psychotropic drugs	1.70 (1.67 to 1.74)	1.50 (1.47 to 1.53)
Potentially serious drug–drug interactions	0.93 (0.91 to 0.95)	0.81 (0.80 to 0.83)
aspirin plus NSAIDs	0.97 (0.94 to 0.99)	0.88 (0.86 to 0.91)
aspirin plus warfarin	0.47 (0.43 to 0.50)	0.42 (0.39 to 0.45)
warfarin plus NSAIDs	0.64 (0.59 to 0.69)	0.60 (0.56 to 0.65)

[a]N = 645,429.
[b]Adjusted for age, education, and number of drugs.

Johnell et al. Ann Pharmacother 2009

Outpatient antibiotic use in Europe and association with resistance: a cross-national database study

*Herman Goossens, Matus Ferech, Robert Vander Stichele, Monique Elseviers, for the ESAC Project Group**

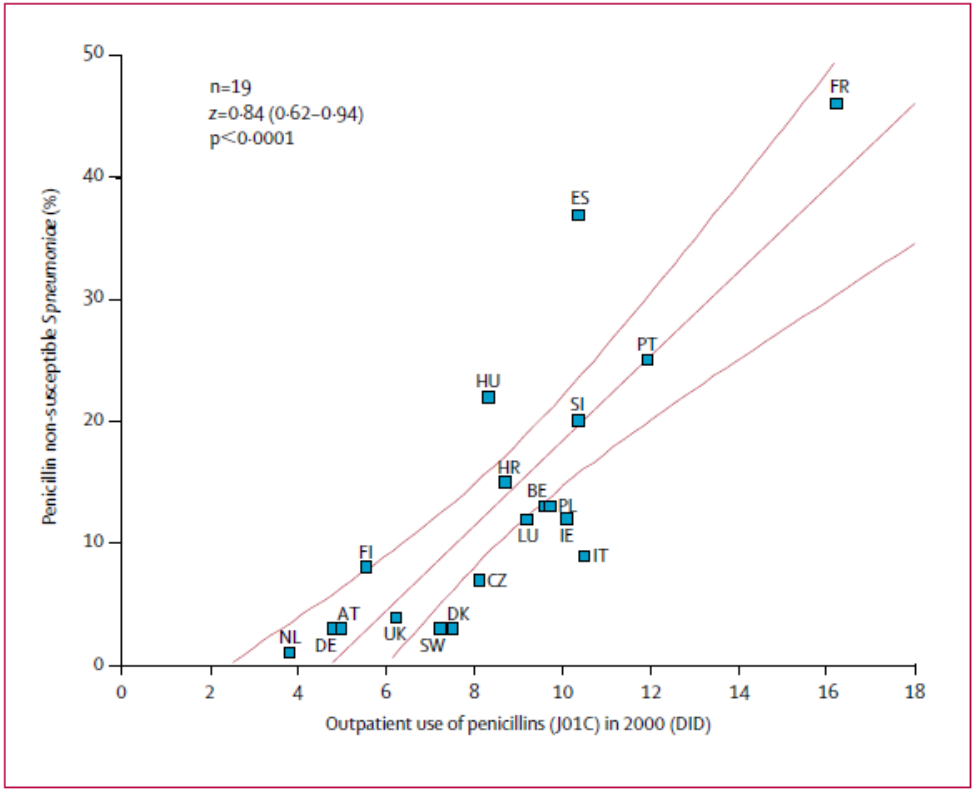


Figure 6: **Correlation between penicillin use and prevalence of penicillin non-susceptible *S pneumoniae***
AT, Austria; BE, Belgium; HR, Croatia; CZ, Czech Republic; DK, Denmark; FI, Finland; FR, France; DE, Germany; HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; NL, The Netherlands; PL, Poland; PT, Portugal; SI, Slovenia; ES, Spain; UK, England only.

Goosens et al. Lancet 2005

ORIGINAL INVESTIGATION

HEALTH CARE REFORM

Drug, Patient, and Physician Characteristics Associated With Off-label Prescribing in Primary Care

Tewodros Eguale, MD, MSc; David L. Buckeridge, MD, PhD; Nancy E. Winslade, PharmD; Andrea Benedetti, PhD; James A. Hanley, PhD; Robyn Tamblyn, PhD

Off-label prescribing analyzed in relation to…

- Drug age
- Drug class
- Approved indication count
- Patient age
- Patient sex
- Charlston Comorbidity Index
- Physician graduation year
- Physician sex
- Physician evidence scale

Eguale et al. Arch Intern Med 2012

Long-term Medication Adherence after Myocardial Infarction: Experience of a Community

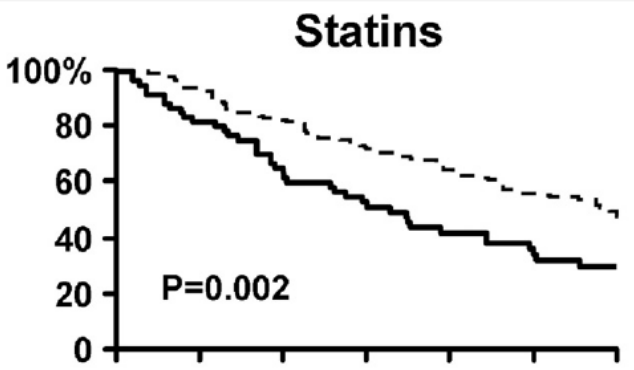
Nilay D. Shah, PhD,[a,b] Shannon M. Dunlay, MD,[c] Henry H. Ting, MD,[b,c] Victor M. Montori, MD,[b,d] Randal J. Thomas, MD,[c] Amy E. Wagie, BS,[a] Véronique L. Roger, MD[c,e]

[a]Division of Health Care Policy and Research, [b]Knowledge and Encounter Research Unit, [c]Division of Cardiovascular Diseases, [d]Division of Endocrinology Diabetes Metabolism and Nutrition, and [e]Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, Minn.

Table 2 Predictors of Medication Discontinuation after Myocardial Infarction

	Statins (n = 219)	
Variable	Hazard Ratio	95% CI
Age (per year increase)	1.01	0.99–1.02
Male sex	0.82	0.58–1.17
Current smoker	1.20	0.81–1.77
Received reperfusion or revascularization therapy	0.96	0.65–1.40
Enrolled in cardiac rehabilitation program	0.66	0.45–0.92
Number of comorbidities*	1.04	0.93–1.16

ACE-I/ARB = angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker
Hazard ratios are from multivariable analyses.
*Determined from comorbidities used to calculate the Charlson comorbidity index.



Shah et al. Am J Med 2009

Qualitative designs

Observation

In depth interviews

Focus groups

Consensus methods

Do patients' expectations influence their use of medications?

Qualitative study

Lisa Dolovich PharmD MSc Kalpana Nair MEd MSc Connie Sellors Lynne Lohfeld PhD
Annie Lee MSc(T) Mitchell Levine MD MSc FRCPC FISPE

Good grief! Eight pills for supper, wonderful! [sarcastic tone] But then I look at it the other way and I say, "Well, without those 8 pills, I can't go for a walk, I can't do the shopping." You're grateful in many ways that the medications are there. (A011-155)

The birth control pill makes it so that I can sort of function in society. Without it, it gets to a point where the frequency of changing a feminine hygiene product would interfere with class or work. So, again, it's something that sort of keeps me a member of society. (B111-81)

Dolovich et al. Can Fam Physician 2008

Whose Job Is It Anyway? Swedish General Practitioners' Perception of Their Responsibility for the Patient's Drug List

Pia Bastholm Rahmner, PhD[1,2,3]
Lars L. Gustafsson, MD, PhD[1,4]
Inger Holmström, RN, PhD[3]
Urban Rosenqvist, MD, PhD[3]
Göran Tomson, MD, PhD[2,5]

Figure 1. Outcome space of internal relationship between 5 categories: the GPs' collective approach to managing responsibility for patient drug lists.

Category D. Different but shared responsibility between GP and patient	
Category E. The patient is responsible for drug information transfer between prescribers	**Category C.** GP is responsible for all prescribed drugs
	Category B. GP is mainly responsible for own prescriptions and how these drugs interact with the current patient drug list
	Category A. GP feels an imposed responsibility from previous prescriber

GP = general practitioner.

Note: Category D is the most comprehensive; it comprises a broader understanding because it includes aspects of the other 4 categories (A, B, C, and E), as well as the patient perspective on drug therapy. In contrast, GPs expressed a more restricted understanding in category A, often excluding aspects from above categories.

Bastholm Rahmner et al. Ann Fam Med 2010

Quasi experimental designs

- Uncontrolled before and after study
- Controlled before and after study
- Time series analysis

Experimental designs

- Randomized controlled trial
- Cluster randomized trial

Controlled before and after study

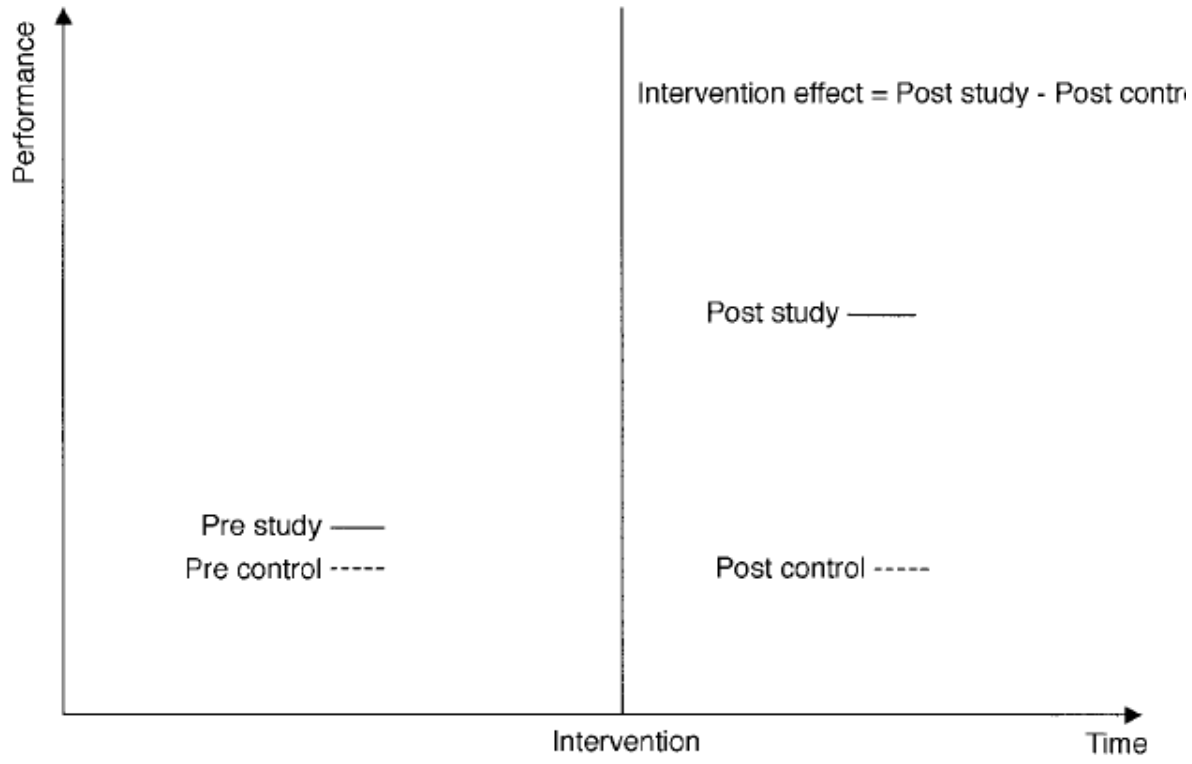


FIGURE 2 *Controlled before and after study*

Grimshaw et al. Fam Pract 2000

Sipilä *et al. BMC Family Practice* 2011, **12**:87
http://www.biomedcentral.com/1471-2296/12/87

BMC Family Practice

RESEARCH ARTICLE Open Access

Change in antihypertensive drug prescribing after guideline implementation: a controlled before and after study

Table 3 Number and proportions of patients who used two or more antihypertensive drugs concurrently and adjusted odds ratios for change

	Intervention				Controls				Intergroup comparison	
	2001	2003	Adjusted* OR (95% CI)	p-value	2001	2003	Adjusted* OR (95% CI)	p-value	Adjusted* OR (95% CI)	p-value
	n (%)				n (%)					
Hypertension	828 (36.8)	1164 (39.2)	1.12 (0.99, 1.25)	0.06	2119 (38.5)	2774 (41.3)	1.13 (1.05, 1.21)	0.002	0.99 (0.86, 1.13)	0.86
CHD	110 (34.4)	164 (37.3)	1.19 (0.87, 1.62)	0.23	292 (30.7)	389 (33.9)	1.10 (0.91, 1.33)	0.33	1.07 (0.75, 1.54)	0.70
Diabetes	144 (47.7)	250 (54.8)	1.33 (0.99, 1.79)	0.06	303 (49.5)	428 (51.7)	1.10 (0.89, 1.36)	0.38	1.22 (0.85, 1.75)	0.28

Prescription data was drawn from the national Prescription Register during a three-month period in 2001 and 2003.

Abbreviations: CHD, coronary heart disease; OR, Odds ratio; CI, confidence interval.

*Within-group analysis: Logistic regression, random effects model (physician as a random effect). Adjusted for patient's age and patient's sex. Reference group: patients with one antihypertensive drug.

**Intergroup analysis: Logistic regression, random effects model (physician as a random effect). A product term between time (after versus before) and group (intervention versus control) was added in the model. Adjusted for patient's age and patient's sex. Reference group: patients with one antihypertensive drug.

Sipilä et al. BMC Fam Pract 2011

Time series analyses

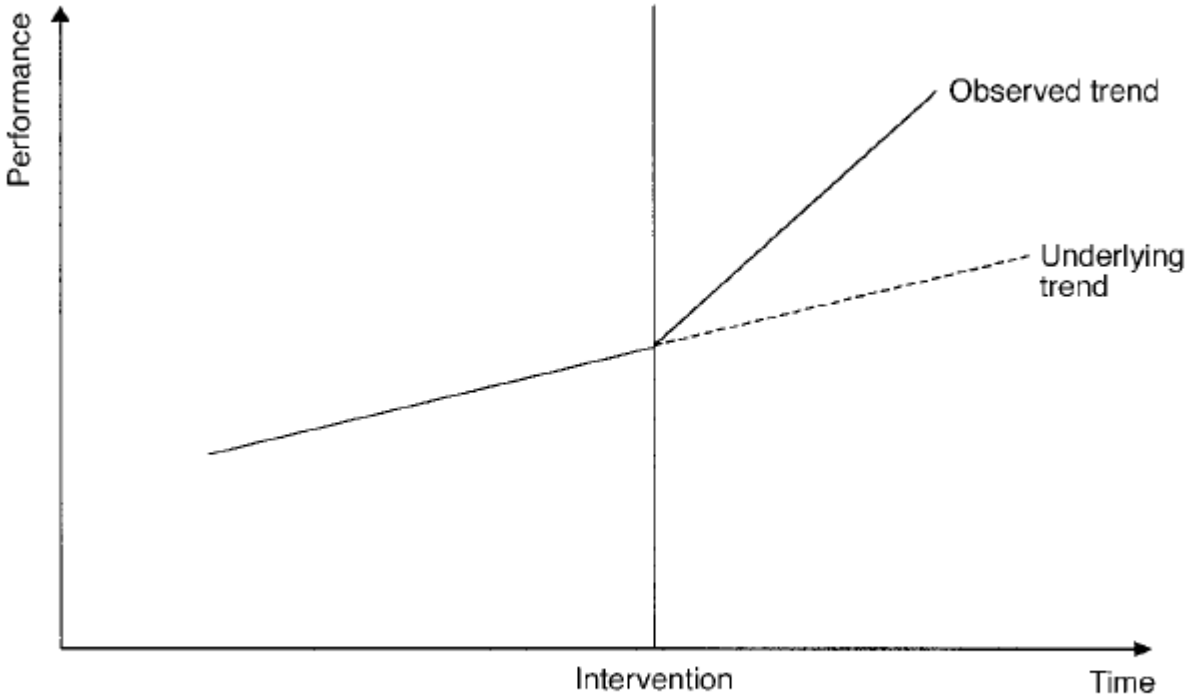


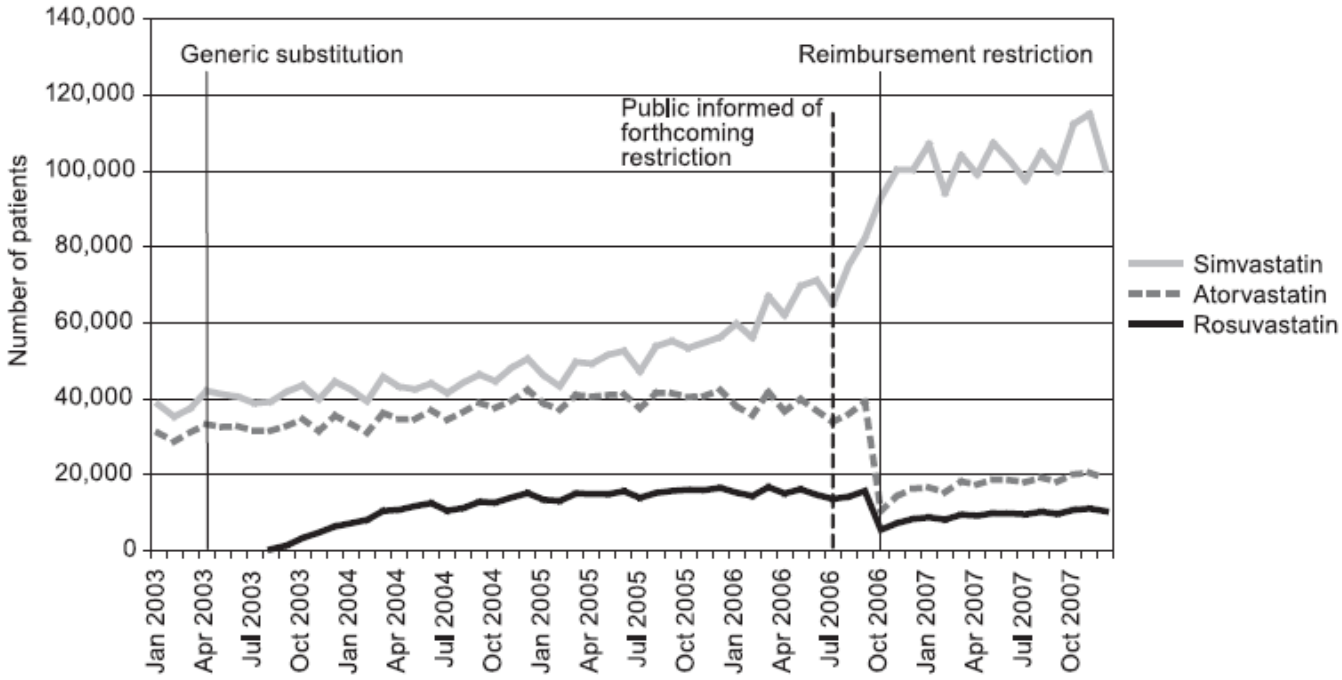
FIGURE 1 *Time series analysis*

Grimshaw et al. Fam Pract 2000

ORIGINAL ARTICLE

Impact of Restricted Reimbursement on the Use of Statins in Finland

A Register-Based Study



Martikainen et al. Med Care 2010

Randomised controlled trials

Scandinavian Journal of Primary Health Care, 2012; 30: 3–9

informa
healthcare

ORIGINAL ARTICLE

Drug treatment in the elderly: An intervention in primary care to enhance prescription quality and quality of life

INGER NORDIN OLSSON[1*], REBECKA RUNNAMO[1,2] & PETER ENGFELDT[1]

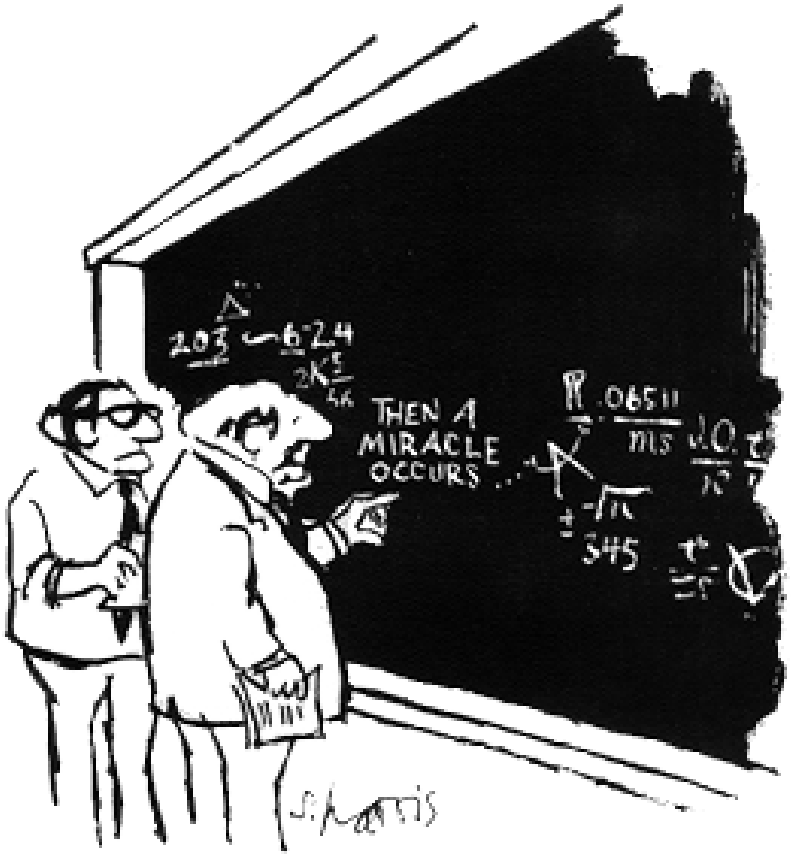
J Antimicrob Chemother 2011; **66**: 2659–2666
doi:10.1093/jac/dkr312 Advance Access publication 5 September 2011

Journal of Antimicrobial Chemotherapy

Can a multifaceted educational intervention targeting both nurses and physicians change the prescribing of antibiotics to nursing home residents? A cluster randomized controlled trial

Eva Pettersson[1*], Åsa Vernby[2], Sigvard Mölstad[3] and Cecilia Stålsby Lundborg[1,4]

Challenges in Drug Utilization Research



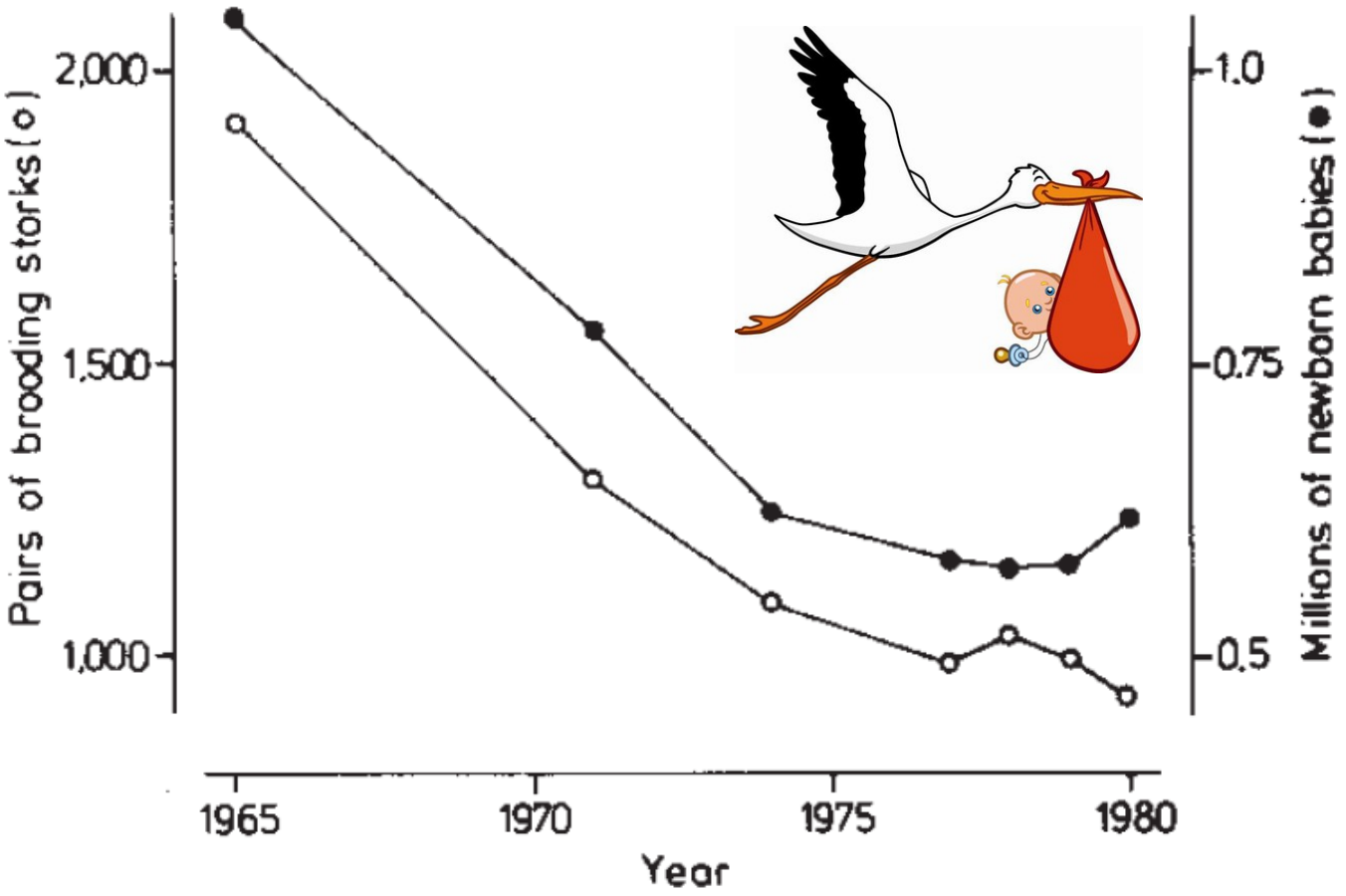
"I think you should be more explicit here in step two."

Challenges in drug utilization research

Descriptive quantitative studies may have problems with poor data validity and limited generalizability

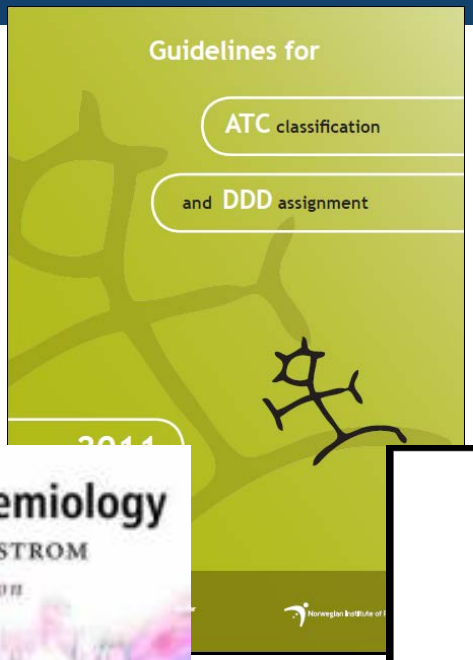
Analytical studies may suffer from the same problems as all pharmacoepidemiological studies, i.e., variation by chance, bias and confounding

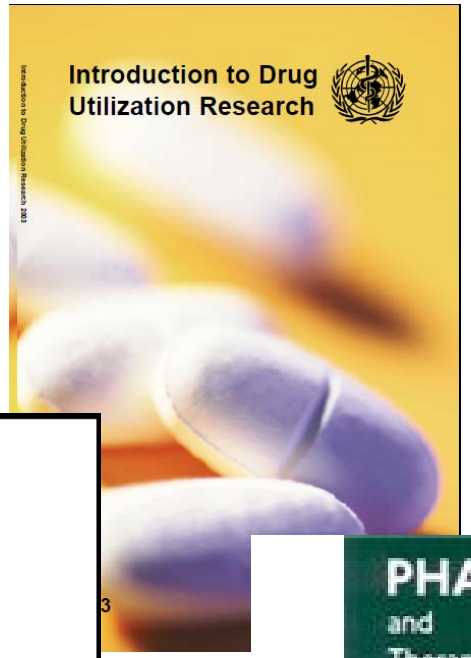
Association between storks and newborn babies in Western Germany 1965-1980

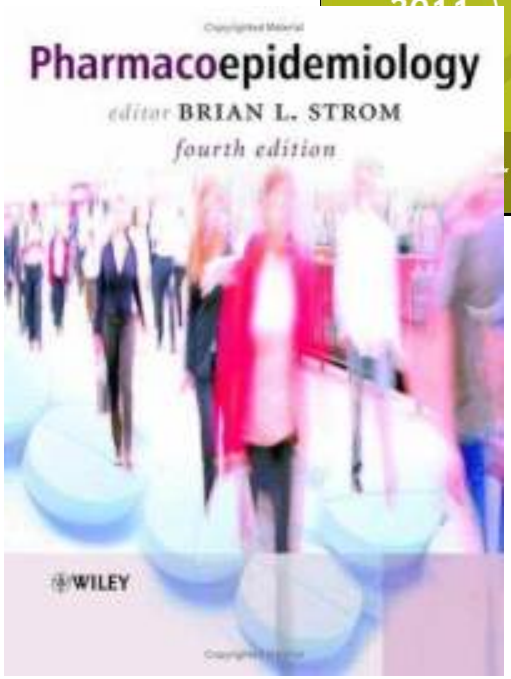


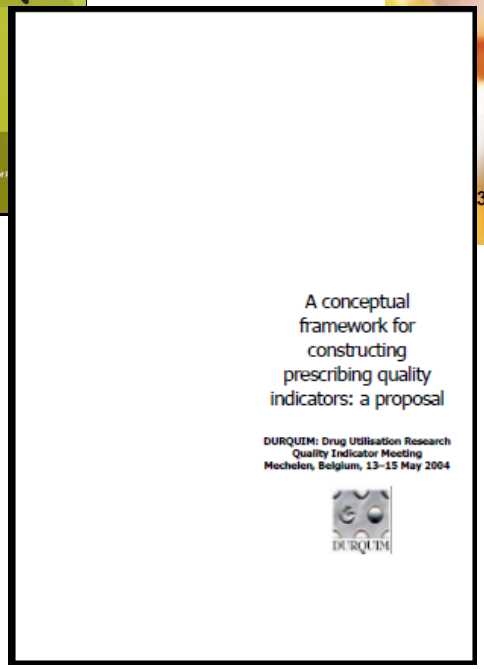
Sies H. Nature 332;495

Resources


Guidelines for
ATC classification
and DDD assignment


Introduction to Drug Utilization Research


Pharmacoepidemiology
editor BRIAN L. STROM
fourth edition
WILEY


A conceptual framework for constructing prescribing quality indicators: a proposal
DURQUIM: Drug Utilisation Research Quality Indicator Meeting
Mechelen, Belgium, 13–15 May 2004
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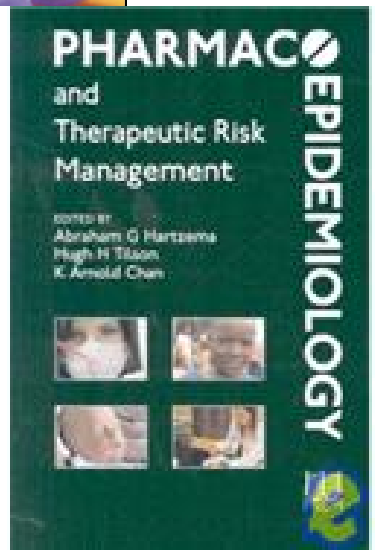
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